

# Abstract

Charles University in Prague, Faculty of Pharmacy in Hradec Kralove

Department of Biochemical Sciences

Candidate: RNDr. Martina Vasatova

Supervisor: prof. RNDr. Milos Tichy, CSc.

Title of Doctoral Thesis: Multimarker approach in diagnosis of cardiovascular diseases with using protein biochips

**Background:** Measurement of biochemical markers of myocardial injury plays an important role in the diagnosis of cardiovascular diseases. Increase in some cardiac biomarkers is one of main diagnostic standard in acute myocardial infarction (AIM) with or without ST elevation (STEMI, NSTEMI). Recently, the European Society of Cardiology, the American College of Cardiology Foundation, the American Heart Association, and the World Heart Federation have published a consensus definition of myocardial infarction (AIM) that includes a detailed guideline for the assessment of biochemical markers in suspected AIM. The principal markers recommended in this setting include cardiac troponins (cTnI and cTnT) as markers of myocardial necrosis and myoglobin (MYO) and creatine kinase MB isoenzyme (CK-MB mass) quantification in the diagnosis of reinfarction. Excluding acute coronary syndromes, myocardial injury may be found in patients with the other cardiovascular diseases, during therapeutic procedures and operations (e.g. percutaneous coronary intervention, radiofrequency ablation etc.) or in treatment with cardiotoxic drug.

**Methods:** For cardiac troponins, in last time, methods on higher analytical sensitivity, so called high-sensitive tests, have been rapidly developed. The armamentarium of cardiac markers has expanded to include several molecules that could be potentially useful for diagnosis of acute coronary syndromes (ACS) and are awaiting validation for routine clinical applications. These novel analytes include glycogen phosphorylase BB isoenzyme (GPBB), heart-type fatty acid-binding protein (h-FABP) and carbonic anhydrase III (CA III).

Evidence Investigator biochip system (Randox) was used to measure levels selected cardiac biomarkers including CKMB mass, cTnI, MYO, h-FABP, CAIII and GPBB. In addition, we have tested a highly sensitive cardiac troponin T (hs-cTnT) assay for Elecsys 2010 analyzer (Roche). Cardiac biomarker levels were measured in cohorts

of healthy blood donors and various patient's groups with cardiovascular diseases (acute myocardial infarction, hypertrophic cardiomyopathy, cardiotoxicity of chemotherapy, radiofrequency ablation).

**Results:** As expected, in AIM patients we have observed statistically significant increases in the serum levels of the measured cardiac biomarkers. In radiofrequency ablation our data indicate that procedure causes the most significant increase of serum hs-cTnT concentration that could be used to monitor myocardial injury. In hypertrophic cardiomyopathy patients, GPBB and h-FABP levels are more sensitive markers compare to troponin I, CKMB mass and myoglobin levels, GPBB level was associated with clinical parameters. Our results suggest that administration of chemotherapy for hematologic malignancies could be associated with myocardial injury manifested by increased release of GPBB from cardiomyocytes.

**Conclusion:** Multianalyte biochip-based assay is applicable for biochemical diagnosis of acute coronary syndromes and may add valuable information to standard single marker assays.